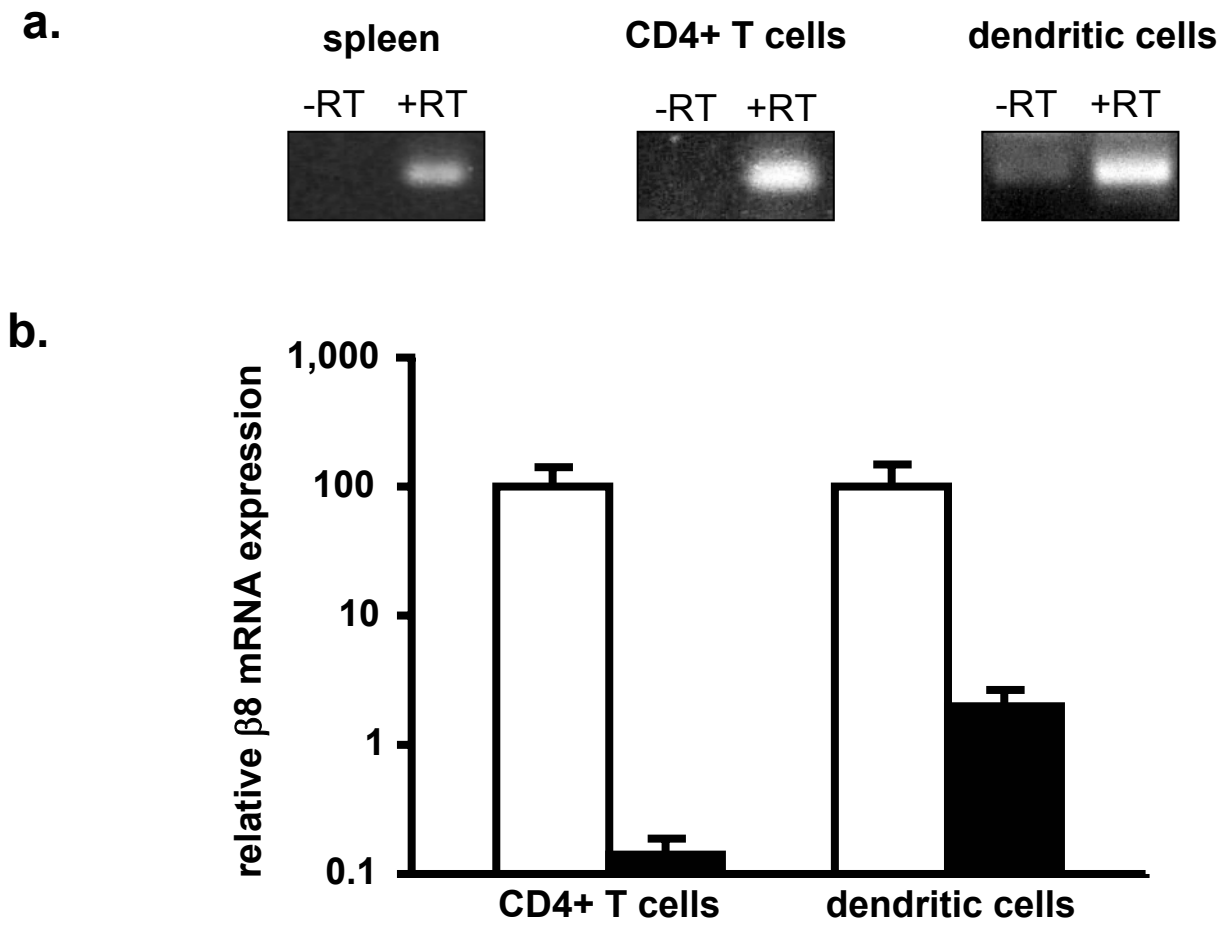
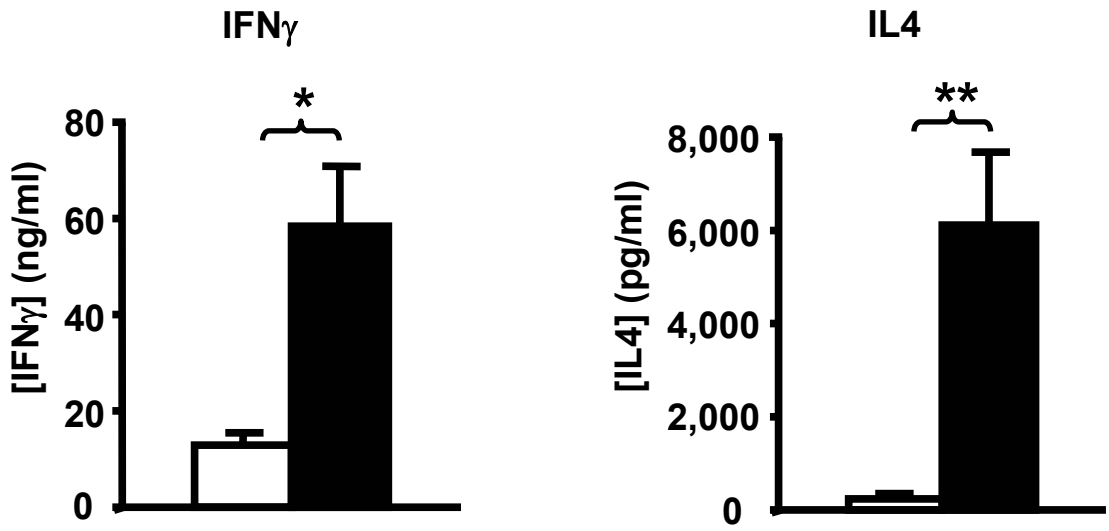
Supplementary Figure 1



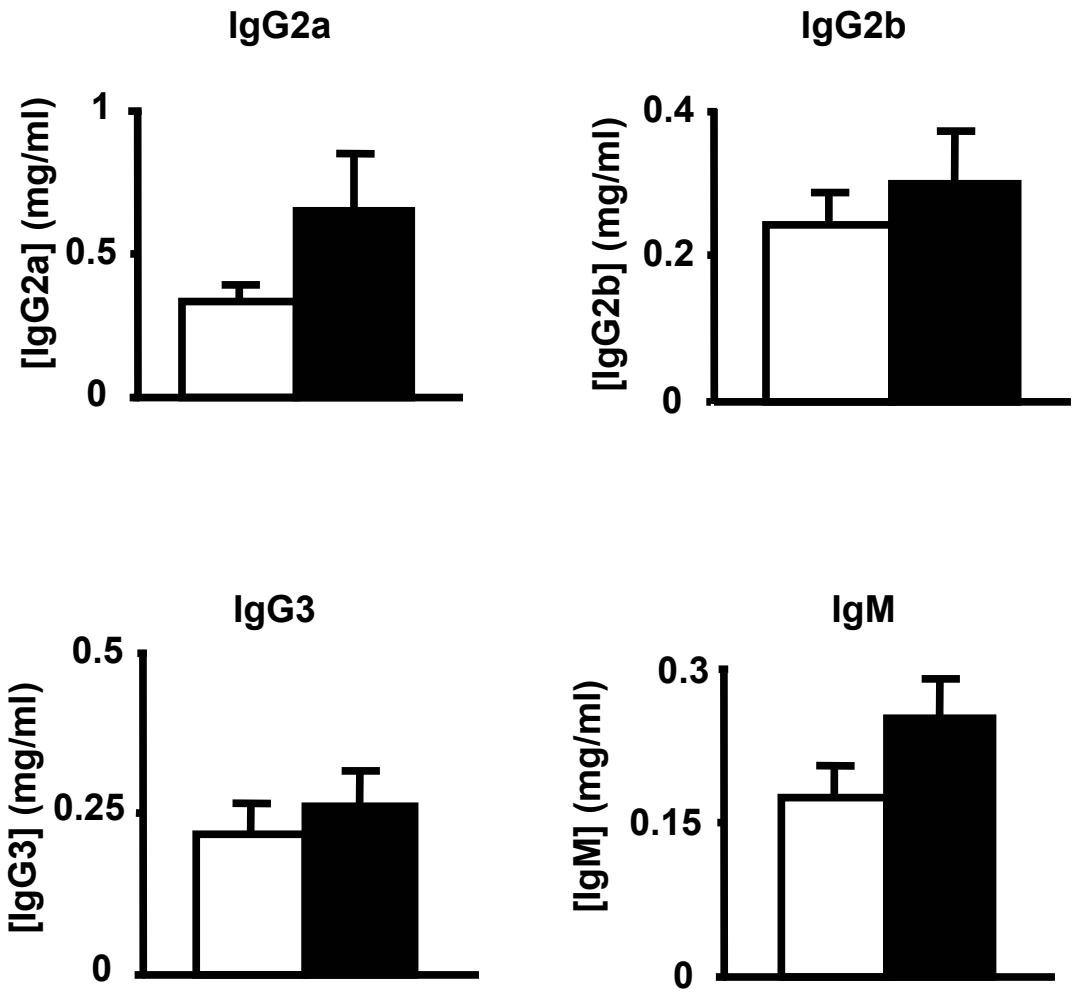
Supplementary Figure 1: β8 integrin is expressed in the immune system of mice, and is efficiently knocked out in CD4+ and dendritic cells in *(Vav1-cre)Itgb8$^{fl/fl}$* mice. (**a**) RNA was purified from either whole spleen, or purified CD4+ T cells and CD11c+ dendritic cells. RNA was reverse transcribed, and cDNA analyzed with primers specific for mouse integrin β8. Control reactions, using cDNA in which reverse transcriptase was not added during reverse transcription (-RT), were analyzed by gel electrophoresis on 2% agarose gels alongside experimental reactions (+RT). (**b**) CD4+ T cell or CD11c+ dendritic cell mRNA isolated from control or *(Vav1-cre)Itgb8$^{fl/fl}$* mice was analyzed for β8 expression by qRT-PCR (white bars = control, black bars = *(Vav1-cre)Itgb8$^{fl/f}$*. Error bars represent SEM (n=3).

Supplementary Figure 2



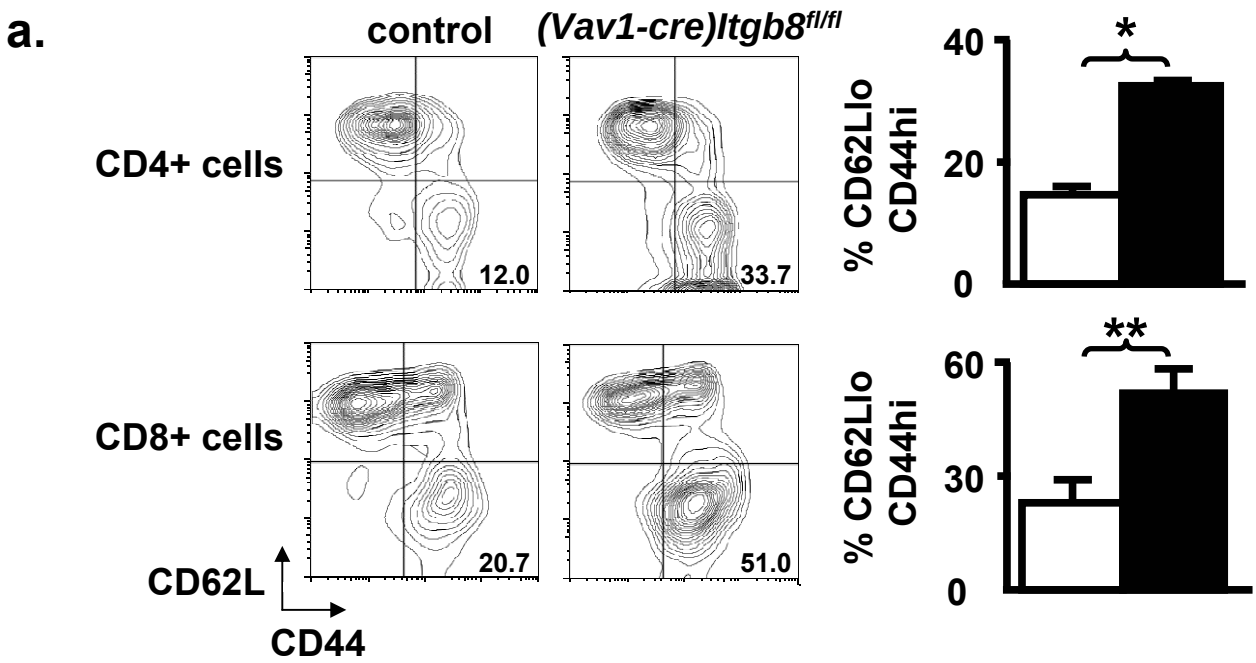
Supplementary Figure 2: *(Vav1-cre)Itgb8$^{fl/fl}$* mice produce elevated levels of IL4 and IFNγ. Splenocytes from 4-6 month old control or *(Vav1-cre)Itgb8$^{fl/fl}$* mice were cultured for 24hrs in the presence of PMA and ionomycin, and levels of IL4 and IFNγ in culture supernatant measured by ELISA (white bars = control, black bars = *(Vav1-cre)Itgb8$^{fl/fl}$*, n=4). Error bars represent SEM (*p= 0.012, **p= 0.0095 (Student T-Test)).

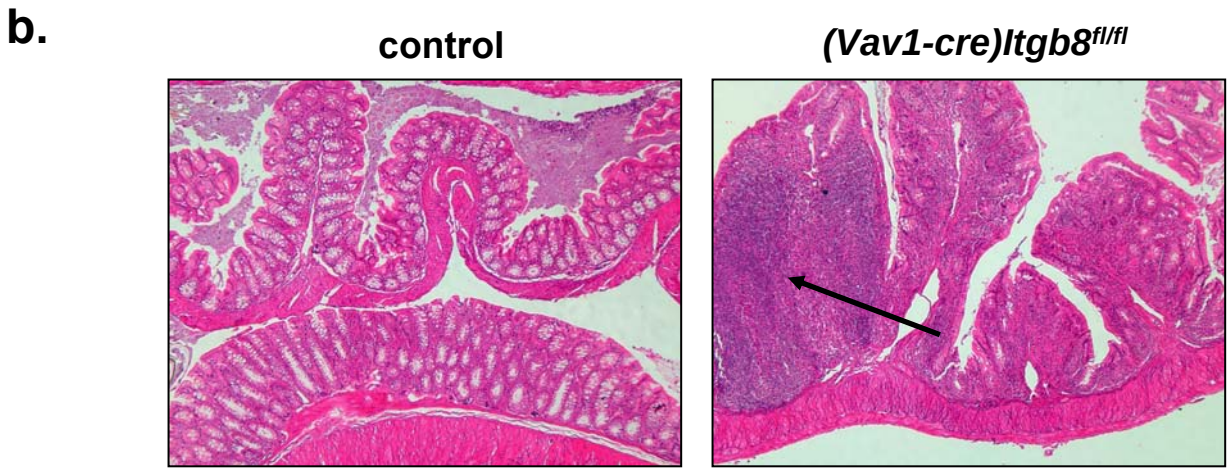
Supplementary Figure 3



Supplementary Figure 3: *(Vav1-cre)Itgb8$^{fl/fl}$* mice show normal serum levels of IgG2a, IgG2b, IgG3 and IgM. Levels of specific Ig isotypes in sera from 4-6 month old mice was analyzed by ELISA (white bars = control, black bars = *(Vav1-cre)Itgb8$^{fl/fl}$* , n=4). Error bars represent SEM (all p values >0.17 (Student T-Test)).

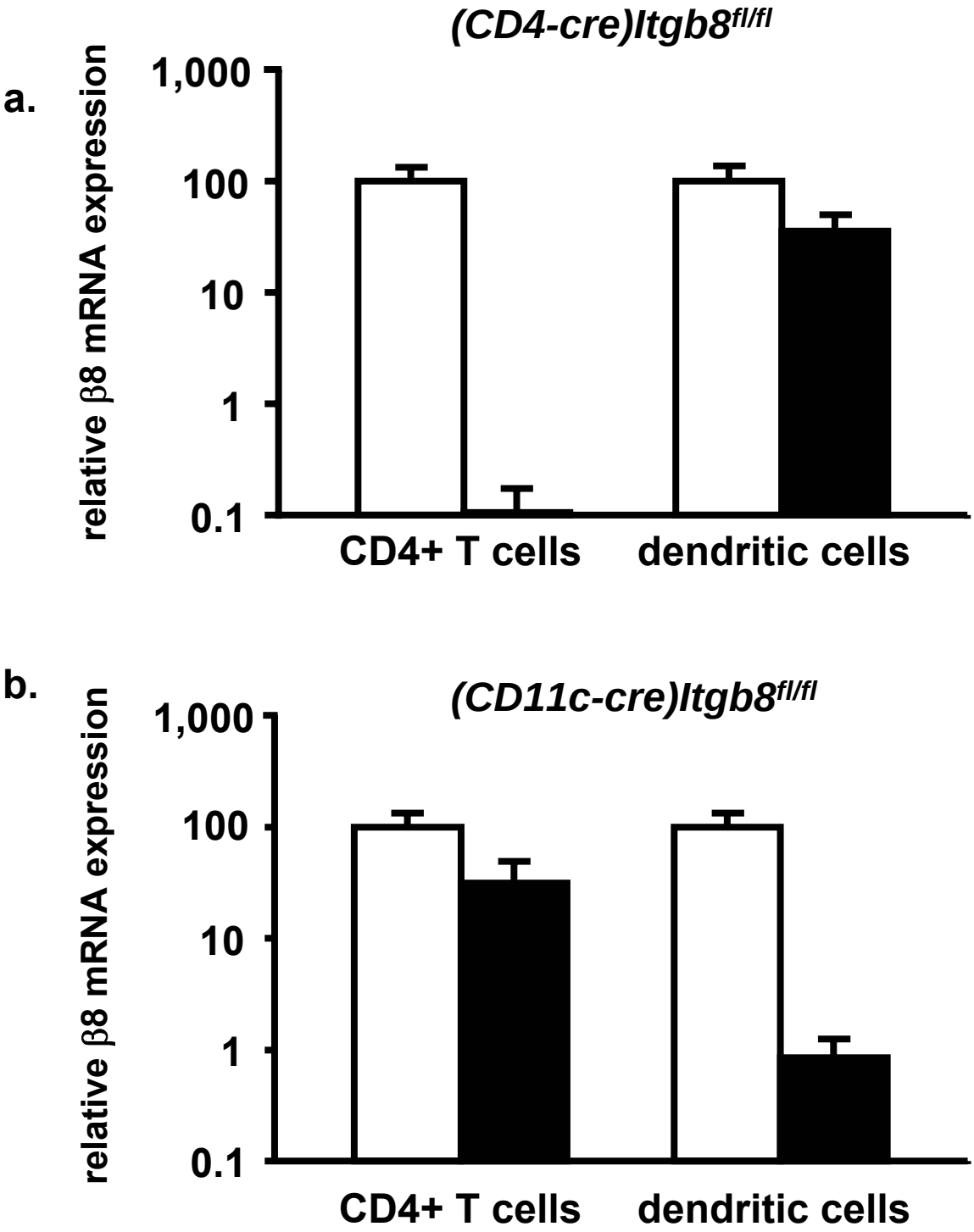
Supplementary Figure 4





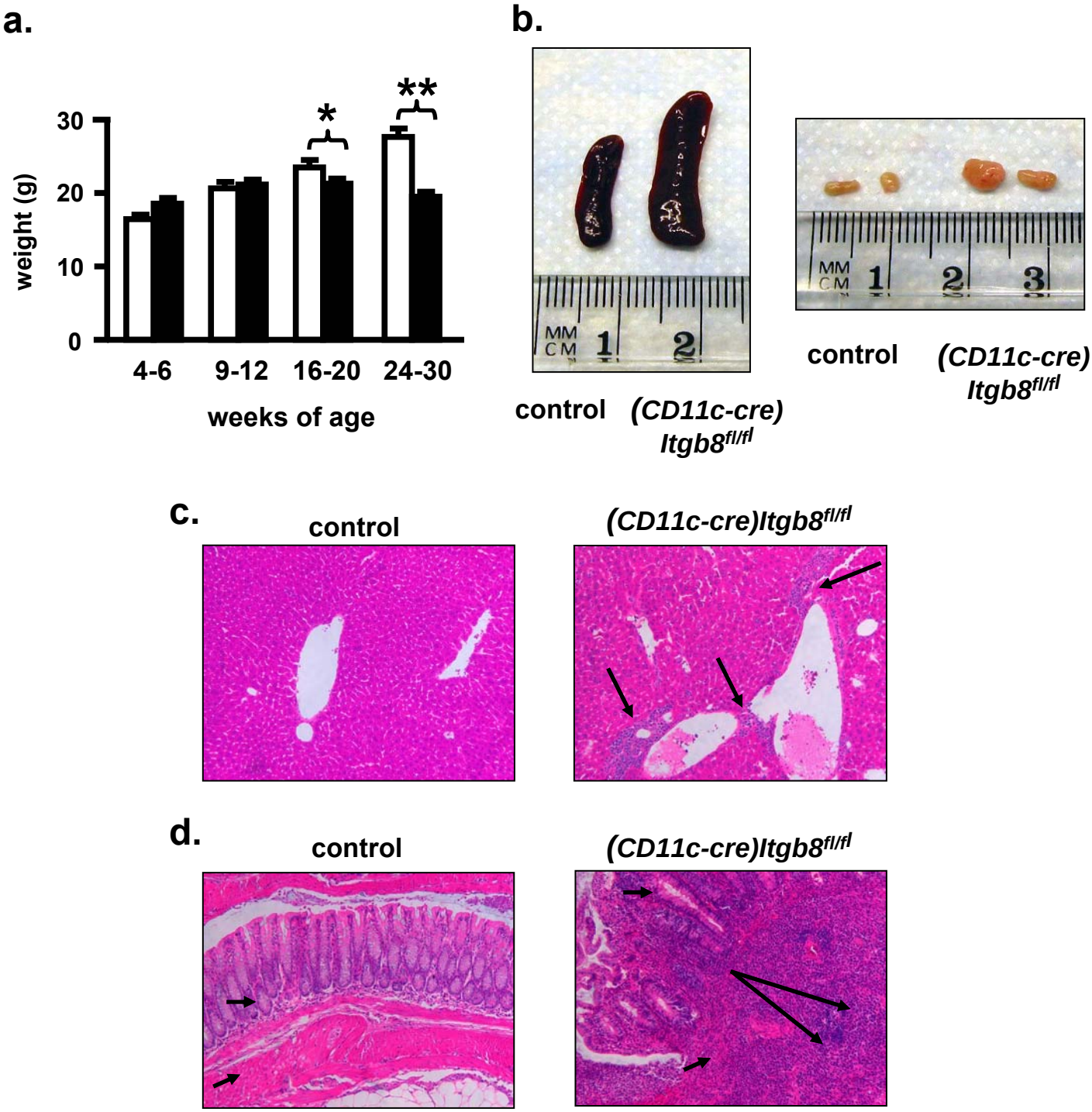
Supplementary Figure 4: Pure strain C57b6 *(Vav1-cre)Itgb8*$^{fl/fl}$ mice develop an identical immune phenotype to *(Vav1-cre)Itgb8*$^{fl/fl}$ mice on a mixed genetic background.
(a) Activated/memory T cells from spleen (CD62L^{low} CD44^{high}) were analyzed by flow cytometry. Representative flow cytometry plots and plotted mean values are shown (white = control, black = *(Vav1-cre)Itgb8*$^{fl/fl}$, n=3, *p= 0.00039, **p=0.031). (b) severe inflammation of the colon (H+E stained sections) in *(Vav1-cre)Itgb8*$^{fl/fl}$ but not control mice. Large arrow indicates cellular infiltration (x50 magnification).

Supplementary Figure 5



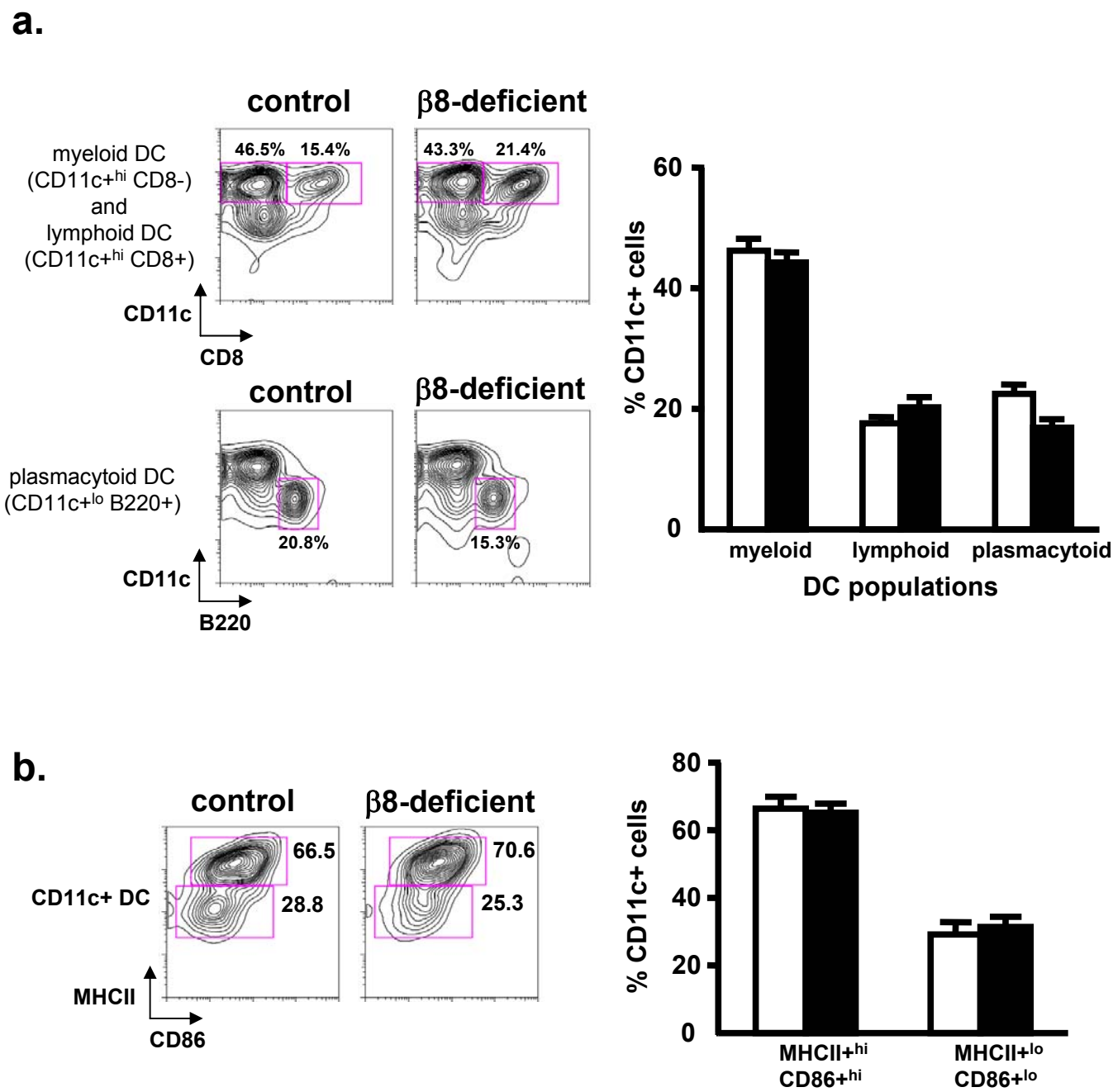
Supplementary Figure 5: *(CD4-cre)Itgb8*$^{fl/fl}$ mice have complete KO of β8 expression in CD4+ T cells, but only partial KO in dendritic cells, whereas *(CD11c-cre)Itgb8*$^{fl/fl}$ mice have complete KO of β8 expression in dendritic cells and only partial KO in CD4+ T cells. CD4+ T cell or CD11c+ dendritic cell mRNA isolated from (a) *(CD4-cre)Itgb8*$^{fl/fl}$ or (b) *(CD11c-cre)Itgb8*$^{fl/fl}$ mice (and controls) was analyzed for β8 expression by qRT-PCR (white bars = control, black bars = *(CD4-cre)Itgb8*$^{fl/fl}$ (a) or *(CD11c-cre)Itgb8*$^{fl/fl}$ (b)). Error bars represent SEM (n=3).

Supplementary Figure 6



Supplementary Figure 6: *(CD11c-cre)Itgb8$^{fl/fl}$* develop an identical age-related autoimmune phenotype to mice lacking β8 on all leukocytes.
Like *(Vav1-cre)Itgb8$^{fl/fl}$* mice, *(CD11c-cre)Itgb8$^{fl/fl}$* mice develop: (**a**) significant weight loss (n=8-10 in each group, *p= 0.0026, **p= 0.000033 (Student T-test)). (**b**) massive enlargement of the spleen and intestinal lymph nodes (organs from 7 month old mice shown). (**c**) severe inflammation of the liver (H+E stained sections, x100 magnification, organs from 7 month old mice. Black arrows indicate cellular accumulations). (**d**) severe inflammation of the colon (H+E stained sections, organs from 6 month old mice, small arrows indicate epithelium and smooth muscle, large arrows indicate cellular infiltration (x50 magnification)).

Supplementary Figure 7



Supplementary Figure 7: Dendritic cells (DCs) lacking β8 integrin expression show normal subpopulation and activation levels. (**a**) Control or β8-deficient CD11c+ DCs from 2-4 month old mice were analyzed by flow cytometry for markers of myeloid DC lineage (CD11c+hi CD8-), lymphoid lineage (CD11c+hi CD8+), and plasmacytoid lineage (CD11c+lo B220+). Representative flow cytometry plots are shown, along with plotted mean values (white bars = control DCs, black bars = β8-deficient DCs, n = 5). Error bars represent SEM. (**b**) Control or β8-deficient CD11c+ DCs from 2-4 month old mice were analyzed for the activation markers MHCII and CD86. Representative flow cytometry plots are shown, along with plotted mean values (white bars = control DCs, black bars = β8-deficient DCs, n = 3). Error bars represent SEM.